

EXHIBIT 5

From: Beach Lawyer <beachlawyer51@hotmail.com>
Sent: Thursday, August 6, 2015 1:08 PM
To: Mark Cheffo
Subject: FW: NEJM Correction

Mark

I am producing this email chain I just received from Sander Greenland who I had previously called regarding the Louik study.

Mark

Subject: Fwd: RE: NEJM Correction
To: beachlawyer51@hotmail.com
From: lesdomes@g.ucla.edu
Date: Thu, 6 Aug 2015 09:39:21 -0700

Mark:

You have asked me for these e-mails - I am producing them on the understanding that they have been produced by the Slone investigators involved below and that they would be subpoenaed by the defense otherwise. - Sander

----- Forwarded Message -----

Subject: RE: NEJM Correction

Date: Mon, 27 Jul 2015 10:29:07 +0000

From: Hernandez-Diaz, Sonia <shernan@hsph.harvard.edu>

To: Sander Greenland <lesdomes@g.ucla.edu>

CC: Mitchell, Allen A <allenmit@bu.edu>, Louik, Carol <clouik@bu.edu>, Werler, Martha M <werler@bu.edu>, Lin, Angela E., M.D. <ALIN@PARTNERS.ORG>

Dear Sander,

I have learnt that an amicus brief can be perceived as part of the litigation. As I mentioned, I would prefer not to get involved in litigations for several reasons.

However, I still agree with the methodological principles and would be happy to sign a letter to the editor or commentary if you decide to move forward with the piece.

All the best,
sonia

From: Hernandez-Diaz, Sonia

Sent: Saturday, July 18, 2015 11:46 AM

To: 'Sander Greenland' <lesdomes@g.ucla.edu>

Cc: Mitchell, Allen A <allenmit@bu.edu>; Louik, Carol <clouik@bu.edu>; Werler, Martha M <werler@bu.edu>; Lin, Angela E., M.D. <ALIN@PARTNERS.ORG>

Subject: RE: NEJM Correction

Hi,

Yes, agree.

I meant with chance just that other studies have not replicated the proposed association (I had in mind the recent BMJ Bayesian analysis by CDC).

But, agree, the interpretation of effect yes/no would be more involved.

Thank you for the manuscripts. I have no experience with litigations (crossing fingers I don't have to) but it is interesting to learn about the challenges.

All the best,
sonia

From: Sander Greenland [<mailto:lesdomes@g.ucla.edu>]

Sent: Friday, July 17, 2015 1:27 PM

To: Hernandez-Diaz, Sonia
Cc: Mitchell, Allen A; Louik, Carol; Werler, Martha M; Lin, Angela E.,M.D.
Subject: Re: NEJM Correction

Thanks Sonia -

Note that I/we are offering no opinion on the effect under study, only trying to promulgate the proper interpretation of the methods.

The issue of the actual effect would be many times more involved.

'Chance' (whatever that means in a nonrandomized study) plays a role in all our results - did you mean that you think the initial associations were selected based on their magnitude and thus overestimate the association (if any)?

With rare exceptions involving blatant harm (I've been in cases with $RR=\infty$, $p=0$, half the exposed and no unexposed ever getting the disease), I have begun limiting my opinions in cases to commentary on proper interpretation of methods, especially regarding the rampant significance-testing abuse - along the lines of the Greenland-Poole Jurimetrics article I sent. The situation with statistics abuse in the courts is scandalous when compared to what is considered the norm for a leading journal like Epidemiology.

Sometimes the opinions I write would actually help the defense, but so far it seems their statistical 'experts' as well as attorneys on both sides largely fail to notice that, so locked in are they onto the magical 0.05 that it's actually amusing.

Best,
Sander

On 7/17/2015 8:54 AM, Hernandez-Diaz, Sonia wrote:

Dear Sander,
I agree with the points you make and would accept your invitation to co-sign the amicus brief with these principles.

However, just to fully disclose my interpretation of the accumulated evidence, I do believe that chance might have played a role in some of the initially reported associations.

All the best,
sonia

From: Sander Greenland [<mailto:lesdomes@g.ucla.edu>]
Sent: Tuesday, July 14, 2015 9:51 PM
To: Mitchell, Allen A
Cc: Louik, Carol; Hernandez-Diaz, Sonia; Werler, Martha M; Lin, Angela E.,M.D.
Subject: Re: NEJM Correction

Dear Allen,

I apologize for not writing you initially, but I asked Sonia and Martha for the information because I was told you were unavailable and I know them both personally. I was then told Carol, not you, had the information. No slight to you was intended and I regret that you took it that way.

I am now surprised and deeply disturbed that you have refused my request, especially since Kimmel did not submit his request to everyone on the paper either, and I can see no labor, confidentiality, legal or embargo issue involved here to justify withholding this tiny bit of information. So your withholding the data seems to me to be a personal slight, as well as an ethical mistake as I will now explain.

In my collaborations we do not need permission to supply such purely statistical details like this to requestors, because we think that should be a matter of public record - especially when the study was paid for by the public (listed on the study are NICHD and NHLBI). Apparently you view these details differently, incommensurable with views that such data are not yours but information which you were paid to obtain and analyze in order to supply vital information to the public - which includes courts and other branches of government.

Your comment about p-values is also disturbing insofar as you say "the slavish worship of the dichotomous p-value is something we have fought fiercely" yet Louik et al. 2007 uses "significance" or its variants to refer to dichotomized P-values no less than 3 times in the abstract and 9 times in the remaining text. I decided to check one of your 2015 studies ("Maternal hypertensive disorders, antihypertensive medication use, and the risk of birth defects: a case-control study") and was pleased to see that statistical "significance" was used only 5 times, so perhaps you will achieve internal victory over dichotomization by 2020. Meanwhile, I've done my share for the cause of extirpating significance abuse in the legal arena and elsewhere, as the 5 attached example articles illustrate.

You responded quickly to Steve Kimmel's inquiry even though his e-mail made clear it was litigation motivated. We all can see exactly how Steve Kimmel used the information - Please read the first page of the attached: he used it precisely for the type of dichotomy abuse you say you decry, quoting your e-mail directly in his defense report. Thus it is your prompt aid to defense which created the need for my request, which was based on what may be seen as Kimmel's misrepresentation of facts which you supplied.

In other words, my request is not a random one for some isolated case, but one produced by your own actions. Thus I find it difficult to comprehend how you can claim to distance yourself in this matter by denying information to a colleague after

your aid to a litigant. And frankly, Allen, if the more precise result would not support his claim of nonsignificance, by refusing requests for this detail you are now abetting defense misrepresentation to the court of your actual results. In any event, the precise results may well become public along with the correspondence via subpoena, so I'm afraid you are already involved in this case, like it or not.

I'd be happy to let our correspondence and the attached correspondence stand (along with the precise result when it becomes available) as a matter of public record for others to infer what principles you were applying and violating in denying my request. However, before this matter goes to public review, I'll propose what I hope is an amicable and constructive solution: I was preparing to submit the information in an *amicus* brief to the court (recall that I am not an expert in this case). Together we could all author this *amicus* brief in which we (rather than discovering attorneys) supply the detail and explain that it should not be interpreted based on whether 1 exactly falls in or out of the interval. I am completely open on the precise wording as long as the crucial information is conveyed to the court but here is how I thought that brief could go (I have omitted citations for now but obviously Modern Epidemiology and writings by me and collaborators would be among them):

It has come to our attention that a supplementary report filed in this matter [cite] has reported that the corrected confidence interval of 1.0-4.0 from the study by Louik et al. (2007) for the adjusted association of sertraline (Zoloft) and septal defects no longer includes 1 and thus cannot be considered "statistically significant."

We hereby wish to advise the court that although this is a technically [inaccurate/accurate] description insofar as the interval expressed with greater precision is $?.??-?.??$, decisions based on the significance or nonsignificance of single studies are inappropriate, as has been widely documented in the methodologic literature [cites]. Among the reasons are that proper combination of statistical results requires the presentation and interpretation of evidence from each study along a continuum, not as a dichotomy of significant/nonsignificant. The latter dichotomy is highly misleading because it discards essential information about how strongly or weakly the evidence from each study supports or conflicts with the hypothesis being tested. A common continuous measure is the P-value, which in this case happens to be 0.0???. Whether it happens to fall slightly above or below the usual 0.05 threshold of "significance" is irrelevant to this measure, for the study alone is not a proper basis for any decision; in particular, statistical tests are designed to be applied to the totality of available statistical evidence, not applied and then combined after the fact. Thus the results of Louik et al. need to be combined with other evidence to

properly evaluate the material as well as statistical significance of the overall evidence.

The need to go beyond statistical significance when considering evidence has been affirmed by a rare unanimous opinion by the Supreme Court of the United States [Matrixx]. We strongly urge the court in the present case to study this decision in detail, and to modify its current application of significance criteria to apply only to overall evidence, not individual studies. Such a modification would bring the deliberations in this case into line with the Supreme Court opinion and also align with current recommendations in the peer-reviewed literature and leading textbooks on evidence synthesis [cites]."

I would be honored if you would join me in creating and filing this brief. Again I intend the invitation to all authors of the original paper who might be interested and in agreement with these points. In fact others in agreement could join if you felt comfortable with that (I was thinking of Ken Rothman in particular).

Sincerely,
Sander

On 7/13/2015 11:09 AM, Mitchell, Allen A wrote:

Dear Sander,

I hope all is well with you.

Carol forwarded me the email exchanges below; since you had initially written to Sonia and Martha, and then Carol, I would have hoped that you would have included me as well.

To respond to your note:

First, let me reflect my personal perspective that the slavish worship of the dichotomous p-value is something we have fought fiercely, including with journals to which we submit our work. In that regard, I was delighted to see that Justice Sotomayor (writing for a unanimous court—how's that for an outlier?) noting the fallacy surrounding devotion to the p-value. While you and I may or may not hold similar views about the role of scientists in litigation, as a matter of longstanding policy we make every effort to avoid becoming engaged in any litigation that involves our work.

Second, our response to Steve's inquiry had nothing at all to do with his involvement in litigation (which he disclosed, though he did not indicate for whom he was working). The simple fact was that he raised a question about a CI we published, and on careful re-examination, we found that we had indeed erred. We submitted a correction to the NEJM, and we provided the corrected information to Steve. As is the case for any of our published work, we cannot control how that information is used, including in judicial proceedings.

We let our publications speak for themselves and do not respond to the infinite number of questions that may be of interest to litigants and that might draw us into these legal proceedings.

Best regards,

Allen

(Please note new telephone number)

Allen A. Mitchell, M.D.

Director, Slone Epidemiology Center

Professor of Epidemiology and Pediatrics

Boston University Schools of Public Health and Medicine

1010 Commonwealth Avenue

Boston, MA 02215

allenmit@bu.edu; **phone 617 206 6210**; fax 617 738 5119

From: Sander Greenland [<mailto:lesdomes@g.ucla.edu>]

Sent: Thursday, July 09, 2015 11:50 AM

To: Hernandez-Diaz, Sonia; Werler, Martha M; Louik, Carol

Subject: Re: correction to

Hi Sonia (and Martha and Carol),

Take a look at the exhibit 82 I sent - as you can see the defense expert obtained the results from Alan on request, and used them to place enormous stock in their "nonsignificance" and the confidence interval excluding or including 1. The e-mail exchange with Alan follows the exxpert's statement to the court.

Statisticians and epidemiologists freely present opinions in these legal documents that pander to the testing fetish even though they wouldn't dare do that in one of our journals (and wouldn't even be allowed to in Epidemiology), and the Supreme Court itself has rejected that standard (see last attachment). Still, the judge in this case puts great stock in the magic 0.05 so I am copying this material to Carol.

Carol, I would be very grateful if you could supply the additional digit to the sertraline-septal defect.

With best wishes and thanks in advance,

Sander

On 7/9/2015 1:42 AM, Hernandez-Diaz, Sonia wrote:

Dear Sander,

Carol Louik run the analyses and provided the estimates. I do not know the decimal points.

I understand this is important for the lawyers and that numbers should be accurate. However, I hope the decision to whether consider Sertraline guilty or not is not based on a decimal point from one observational study. Please see the BMJ publication from today concluding there are no increased risks associated with Sertraline. This topic is the Cape Horn of epidemiologic (conflicting) evidence, I am so glad you are involved in the discussion.

All the best,
Sonia

From: Sander Greenland [<mailto:lesdomes@g.ucla.edu>]

Sent: Wednesday, July 08, 2015 4:02 PM

To: Hernandez-Diaz, Sonia; Werler, Martha M

Subject: correction to

Dear Sonia and Martha,

Sorry to bother you with this request, but I got a call from a plaintiff lawyer (Mark Robinson) who consults me on occasion, this time on in a case involving sertraline and septal defects. I'm told I am not a named expert in this case, but he wanted to know if the statistical significance changed due to the correction to the odds-ratio estimate of 2.0 (1.2, 4.0) highlighted in Table 2 of the attached 2007 article on which you are coauthors.

The defense expert, Steve Kimmel, had contacted Alan Mitchell last month about it and got back the correction shown in the attached e-mail exchange.

Alan supplied the defense expert with the correction showing 2.0 (1.0,4.0). Unsurprisingly, the big question it has raised is what are the results to two digits past the decimal point, particularly what is the lower limit out to one more digit?

Alan said in the e-mails to Kimmel that he would be consulting with his coauthors, so I am writing to ask if either of you can state the estimate in more detail?

Again, apologies for bothering you with this request, but I was told Alan is away right now, and I am curious myself about the answer given the capital that Kimmel seems to

have made of it (as you can see in the attached exhibit).
I hope it is an easy question to answer given that Alan mentioned having retrieved the original files in his response to Kimmel.

Thanking you in advance,
All the Best,
Sander